

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 1 | 2179 | fibroblast and 3T3 | USPAT | 2001/10/18 08:48 |
| 2 | 1250 | (fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/18 08:49 |
| 3 | 1250 | (fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/18 08:49 |
| 4 | 220 | fibroblast with (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/21 13:04 |
| 5 | 131 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$) | USPAT | 2001/10/18 09:00 |
| 6 | 52 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$)) and (extracellular matrix and adhesion) | USPAT | 2001/10/21 12:39 |
| 7 | 13 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$)) and (matrix and adhesion) | USPAT | 2001/10/21 12:38 |
| 8 | 1092 | matrix with cell with (growth or proliferation) | USPAT | 2002/10/16 13:38 |
| 9 | 101 | (matrix with cell with (growth or proliferation)) and ((fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death)) | USPAT | 2001/10/18 09:09 |
| 10 | 450 | fibroblast with (matrix or scaffold) | USPAT | 2001/10/18 09:09 |
| 11 | 168 | (fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation)) | USPAT | 2001/10/21 13:06 |
| 12 | 104 | ((fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis) | USPAT | 2002/10/11 14:28 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 13 | 41 | ((fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis)) and ((matrix or scaffold) and adhesion and proliferation) | USPAT | 2001/10/18 09:11 |
| 14 | 2 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and \$radiat\$ and (extracellular adj1 matrix and adhesion) | USPAT | 2001/10/21 12:44 |
| 15 | 0 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and \$radiat\$ and (extracellular adj1 matrix and adhesion)) and 3t3 | USPAT | 2001/10/21 12:44 |
| 16 | 220 | fibroblast with (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/21 12:44 |
| 17 | 51 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and 3t3 | USPAT | 2001/10/21 12:45 |
| 18 | 14 | culture with keratinocyte with fibroblast | USPAT | 2002/04/05 09:16 |
| 19 | 53 | fibroblast with culture with (matrix or medium) with cell with (growth or proliferation) | USPAT | 2002/04/05 09:49 |
| 20 | 1152 | (epithelial or hepatic) with culture | USPAT | 2002/04/05 09:21 |
| 21 | 3 | (fibroblast with culture with matrix) and ((epithelial or hepatic) with culture) | USPAT | 2002/04/05 09:21 |
| 22 | 19 | fibroblast with culture with matrix | USPAT | 2002/04/05 09:29 |
| 23 | 0 | method with make with matrix with fibroblast | USPAT | 2002/04/05 09:50 |
| 24 | 0 | method with make with matrix with collagen | USPAT | 2002/04/05 09:53 |
| 25 | 2910 | collagen with matrix | USPAT | 2002/04/05 09:53 |
| 26 | 1190 | culture with skin | USPAT | 2002/04/05 09:53 |
| 27 | 182 | (collagen with matrix) and (culture with skin) | USPAT | 2002/04/05 09:53 |
| 28 | 51 | collagen with matrix with (prepare or make) | USPAT | 2002/04/05 09:54 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 29 | 694 | ((cell with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis) | USPAT | 2002/10/11 14:34 |
| 30 | 36 | ((cell with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis).ab. | USPAT | 2002/10/11 14:31 |
| 31 | 1384 | cell with (matrix or scaffold or lattice).ab. | USPAT | 2002/10/11 14:32 |
| 32 | 85 | (cell with (matrix or scaffold or lattice).ab.) and growth.ab. | USPAT | 2002/10/11 14:32 |
| 33 | 1693 | cell with (secret\$3 or produc\$4) with (matrix or scaffold) | USPAT | 2002/10/11 14:36 |
| 34 | 1816 | cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice) | USPAT | 2002/10/11 14:47 |
| 35 | 340 | (cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice)) and ((kill\$ or destroy\$ or inhibit adj growth) with cell\$) | USPAT | 2002/10/11 14:53 |
| 36 | 266 | (cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice)) and ((kill\$ or destroy\$ or inhibit adj growth) with cells) | USPAT | 2002/10/11 14:53 |
| 37 | 115 | cell with secrete with (matrix scaffold lattice) | USPAT | 2002/10/16 09:51 |
| 38 | 1 | "4485096".PN. | USPAT | 2002/10/16 09:46 |
| 39 | 23 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN. | USPAT | 2002/10/16 09:50 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|--|---------------------|
| 40 | 0 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (cell with secrete with (matrix scaffold lattice)) | USPAT | 2002/10/16 09:51 |
| 41 | 0 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (secrete with (matrix scaffold lattice)) | USPAT | 2002/10/16 09:52 |
| 42 | 149 | cell with secrete with (matrix scaffold lattice) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/10/16 09:52 |
| 43 | 19 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (matrix scaffold lattice) | USPAT | 2002/10/16 09:54 |
| 44 | 1736 | (matrix scaffold lattice) with cell with (growth or culture or proliferation) | USPAT | 2002/10/16 09:55 |
| 45 | 898 | ((matrix scaffold lattice) with cell with (growth or culture or proliferation)) and fibroblast | USPAT | 2002/10/16 09:56 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 46 | 7 | ((matrix scaffold lattice) with cell with (growth or culture or proliferation)) and (fibroblast with (kill\$4 or destroy or lethal\$2)) | USPAT | 2002/10/16 09:56 |
| 47 | 9 | fibroblast with (matrix or lattice or scaffold) with keratinocyte | USPAT | 2002/10/16 12:26 |
| 48 | 556 | fibroblast with (matrix or lattice or scaffold) | USPAT | 2002/10/16 12:26 |
| 49 | 16 | (fibroblast with (matrix or lattice or scaffold)) same keratinocyte | USPAT | 2002/10/16 12:27 |
| 50 | 8 | hepatic adj1 cells with keratinocytes | USPAT | 2002/10/16 13:37 |
| 51 | 1309 | matrix with cell with (growth or proliferation) | USPAT | 2002/10/16 13:38 |
| 52 | 1 | matrix with cell with (growth or proliferation) with (hepatic or liver) adj1 cells | USPAT | 2002/10/16 13:38 |

US-PAT-NO: 5556645
DOCUMENT-IDENTIFIER: US 5556645 A
TITLE: Methods of enhancing wound healing and tissue repair
DATE-ISSUED: September 17, 1996

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP | CODE | COUNTRY |
|------------------|----------|-------|-------|------|---------|
| Bockman; Richard | New York | NY | 10021 | | N/A |
| Guidon; Peter | Union | NJ | 07083 | | N/A |

APPL-NO: 08/ 430142
DATE FILED: April 26, 1995

PARENT-CASE:

This application is a continuation of application Ser. No. 07/910,118, filed on Sep. 14, 1992, now abandoned; which is a continuation in part of Ser. No. 07/464,361, filed as PCT/US90/06606, Nov. 13, 1990 published as WO91/10437, Jul. 25, 1991 now abandoned.

INT-CL: [06] A61K033/24,A61K031/28
US-CL-ISSUED: 424/650, 514/492
US-CL-CURRENT: 424/650, 514/492
FIELD-OF-SEARCH: 424/650; 514/492

REF-CITED:**U.S. PATENT DOCUMENTS**

| PAT-NO | ISSUE-DATE | PATENTEE-NAME | US-CL |
|----------------|---------------|---------------------|-----------------|
| <u>4529593</u> | July 1985 | Warrell, Jr. et al. | 424/650 N/A N/A |
| <u>4686104</u> | August 1987 | Bockman et al. | 424/650 N/A N/A |
| <u>4704277</u> | November 1987 | Bockman et al. | 424/650 N/A N/A |
| <u>4882166</u> | November 1989 | Graham et al. | 424/462 N/A N/A |

FOREIGN PATENT DOCUMENTS

| FOREIGN-PAT-NO | PUBN-DATE | COUNTRY | US-CL |
|----------------|-----------|---------|-------|
| 62230648A | June 1987 | JP | |

OTHER PUBLICATIONS Bergkvist et al., "The Risk of Breast Cancer after Estrogen-Progestin Replacement", New England Journal of

Medicine, 321:293-297 (1989).

Centrella et al., "Transforming Growth Factor .beta. is a Bifunctional Regulator of Eplication and Collagen Synthesis in Osteoblast-enriched Cell Cultures from Fetal Rat Bone", The Journal of Biological Chemistry, 262:2869-2874 (1987).

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ART-UNIT: 125

PRIMARY-EXAMINER: Weddington; Kevin E.

ABSTRACT:

Skin, connective and support tissue repair is enhanced and augmented by administering pharmaceutically acceptable gallium-containing compounds in amounts sufficient to provide therapeutic levels of elemental gallium. Gallium-containing compounds mimic the effects of endogenous growth factors to induce cells within these tissues to produce new matrix by increasing the formation of critical structural matrix proteins responsible for skin, support and connective tissue repair, maintenance and augmentation. Gallium-containing compounds are suitable for a variety of applications in wound healing, including dermatologic and cosmetic skin repair, bone fracture repair and successful bonding of implanted tissue grafts and connective and support tissue prostheses. The unique ability of the gallium-containing compounds to increase new matrix component formation and favorably alter the proliferation of specific cell types needed for tissue repair is separate and distinct from gallium's inhibitory activity on matrix-resorbing cells such as bone-resorbing osteoclasts.

10 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Detailed Description Text - DETX:

Increasing keratinocyte proliferation means that wound healing is accelerated. The protective barrier over the skin wound is thus

established earlier allowing subsequent healing to proceed in a protected and sterile environment. Wound infection due to inadequate sealing of the wound is probably one of the major impediments to wound healing. Coupled with known enhancement of fibroblast production of key matrix components, gallium-containing compound treatment of skin wounds greatly facilitates and accelerates wound healing.

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|----|------|---|-------|---------------------|
| 1 | 2179 | fibroblast and 3T3 | USPAT | 2001/10/18 08:48 |
| 2 | 1250 | (fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/18 08:49 |
| 3 | 1250 | (fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/18 08:49 |
| 4 | 220 | fibroblast with (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/21 13:04 |
| 5 | 131 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$) | USPAT | 2001/10/18 09:00 |
| 6 | 52 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$)) and (extracellular matrix and adhesion) | USPAT | 2001/10/21 12:39 |
| 7 | 13 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and (freez\$ or dry\$ or \$radiat\$)) and (matrix and adhesion) | USPAT | 2001/10/21 12:38 |
| 8 | 1092 | matrix with cell with (growth or proliferation) | USPAT | 2001/10/18 09:04 |
| 9 | 101 | (matrix with cell with (growth or proliferation)) and ((fibroblast and 3T3) and (kill\$ or cytotoxic or apoptosis or death)) | USPAT | 2001/10/18 09:09 |
| 10 | 450 | fibroblast with (matrix or scaffold) | USPAT | 2001/10/18 09:09 |
| 11 | 168 | (fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation)) | USPAT | 2001/10/21 13:06 |
| 12 | 104 | ((fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis) | USPAT | 2002/10/11 14:28 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 13 | 41 | ((fibroblast with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis)) and ((matrix or scaffold) and adhesion and proliferation) | USPAT | 2001/10/18 09:11 |
| 14 | 2 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and \$radiat\$ and (extracellular adj1 matrix and adhesion) | USPAT | 2001/10/21 12:44 |
| 15 | 0 | ((fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and \$radiat\$ and (extracellular adj1 matrix and adhesion)) and 3t3 | USPAT | 2001/10/21 12:44 |
| 16 | 220 | fibroblast with (kill\$ or cytotoxic or apoptosis or death) | USPAT | 2001/10/21 12:44 |
| 17 | 51 | (fibroblast with (kill\$ or cytotoxic or apoptosis or death)) and 3t3 | USPAT | 2001/10/21 12:45 |
| 18 | 14 | culture with keratinocyte with fibroblast | USPAT | 2002/04/05 09:16 |
| 19 | 53 | fibroblast with culture with (matrix or medium) with cell with (growth or proliferation) | USPAT | 2002/04/05 09:49 |
| 20 | 1152 | (epithelial or hepatic) with culture | USPAT | 2002/04/05 09:21 |
| 21 | 3 | (fibroblast with culture with matrix) and ((epithelial or hepatic) with culture) | USPAT | 2002/04/05 09:21 |
| 22 | 19 | fibroblast with culture with matrix | USPAT | 2002/04/05 09:29 |
| 23 | 0 | method with make with matrix with fibroblast | USPAT | 2002/04/05 09:50 |
| 24 | 0 | method with make with matrix with collagen | USPAT | 2002/04/05 09:53 |
| 25 | 2910 | collagen with matrix | USPAT | 2002/04/05 09:53 |
| 26 | 1190 | culture with skin | USPAT | 2002/04/05 09:53 |
| 27 | 182 | (collagen with matrix) and (culture with skin) | USPAT | 2002/04/05 09:53 |
| 28 | 51 | collagen with matrix with (prepare or make) | USPAT | 2002/04/05 09:54 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|---|-------|---------------------|
| 29 | 694 | ((cell with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis) | USPAT | 2002/10/11 14:34 |
| 30 | 36 | ((cell with (matrix or scaffold)) and (matrix with cell with (growth or proliferation))) and (cytotoxic or death or kill\$ or apoptosis).ab. | USPAT | 2002/10/11 14:31 |
| 31 | 1384 | cell with (matrix or scaffold or lattice).ab. | USPAT | 2002/10/11 14:32 |
| 32 | 85 | (cell with (matrix or scaffold or lattice).ab.) and growth.ab. | USPAT | 2002/10/11 14:32 |
| 33 | 1693 | cell with (secret\$3 or produc\$4) with (matrix or scaffold) | USPAT | 2002/10/11 14:36 |
| 34 | 1816 | cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice) | USPAT | 2002/10/11 14:47 |
| 35 | 340 | (cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice)) and ((kill\$ or destroy\$ or inhibit adj growth) with cell\$) | USPAT | 2002/10/11 14:53 |
| 36 | 266 | (cell with (secret\$3 or produc\$4) with (matrix or scaffold or lattice)) and ((kill\$ or destroy\$ or inhibit adj growth) with cells) | USPAT | 2002/10/11 14:53 |
| 37 | 115 | cell with secrete with (matrix scaffold lattice) | USPAT | 2002/10/16 09:51 |
| 38 | 1 | "4485096".PN. | USPAT | 2002/10/16 09:46 |
| 39 | 23 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN. | USPAT | 2002/10/16 09:50 |

| | Hits | Search Text | DBs | Time Stamp |
|----|------|--|--|---------------------|
| 40 | 0 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (cell with secrete with (matrix scaffold lattice)) | USPAT | 2002/10/16 09:51 |
| 41 | 0 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (secrete with (matrix scaffold lattice)) | USPAT | 2002/10/16 09:52 |
| 42 | 149 | cell with secrete with (matrix scaffold lattice) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/10/16 09:52 |
| 43 | 19 | ((("4485096") or ("4485097") or ("4501815") or ("4505266") or ("4642292") or ("4645669") or ("4661111") or ("4776853") or ("4795459") or ("4801299") or ("4837285") or ("4902508") or ("4917890") or ("4935000") or ("4950483") or ("4956178") or ("4969912") or ("4981841") or ("5024841") or ("5043426") or ("5110604") or ("5192312") or ("5262403"))).PN.) and (matrix scaffold lattice) | USPAT | 2002/10/16 09:54 |
| 44 | 1736 | (matrix scaffold lattice) with cell with (growth or culture or proliferation) | USPAT | 2002/10/16 09:55 |
| 45 | 898 | ((matrix scaffold lattice) with cell with (growth or culture or proliferation)) and fibroblast | USPAT | 2002/10/16 09:56 |

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| 46 | 7 | ((matrix scaffold lattice) with cell with (growth or culture or proliferation)) and (fibroblast with (kill\$4 or destroy or lethal\$2)) | USPAT | 2002/10/16 09:56 |
| 47 | 9 | fibroblast with (matrix or lattice or scaffold) with keratinocyte | USPAT | 2002/10/16 12:26 |
| 48 | 556 | fibroblast with (matrix or lattice or scaffold) | USPAT | 2002/10/16 12:26 |
| 49 | 16 | 12 same keratinocyte | USPAT | 2002/10/16 12:27 |